## REMARKS

This amendment is submitted in response to the Office Action mailed 15 December 2008, in connection with the above-identified application (hereinafter, the "Office Action"). The Office Action provided a three-month shortened statutory period in which to respond, ending on 15 March 2009. Accordingly, this amendment is timely submitted. The Commissioner is hereby authorized to charge Deposit Account No. 50-4498 in the name of Nestle Nutrition for any fees that maybe deemed owed or credit any overpayment.

The Applicant has fully considered the Office Action and cited references and submits this Reply and Amendment in response to the outstanding rejections. Reconsideration of the application for patent is requested. Applicants do not acquiesce in the correctness of the rejections or objections and reserve the right to present specific arguments regarding any rejected or objected-to claims not specifically addressed. Further Applicants reserve the right to pursue the full scope of the subject matter of the claims in a subsequent patent application that claims priority to the instant application.

Claims 1-4, 6-14 and 16-28 are currently pending. Claims 6, 12 and 18-22 were previously withdrawn. Claims 5, 15 and 29 were previously canceled. In the Office Action, Claims 3, 16 and 25 are rejected under 35 U.S.C. §112; and Claims 1-4, 6-14 and 16-28 are rejected under 35 U.S.C. §103. In response Claims 3, 17 and 25 have been amended. These amendments do not add new matter. In view of the amendments and/or for the reasons set forth below, Applicant respectfully submits that the rejections should be withdrawn.

In the Office Action, Claims 3, 16 and 25 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Patent Office asserts that it is unclear how having at least 25% of leucine would lead to a ratio of the intact protein to leucine ranging from about 10:1 to about 1:10. In response, Applicant has amended Claims 3 and 25 to remove the ratio of the intact protein to leucine ranging from about 10:1 to about 1:10 and clarify the percentage basis for leucine.

The Patent Office also asserts that it is unclear how about 36 g to about 59 g of total essential amino acids and/or conditionally essential amino acids per serving would give a ratio from about 0.60 to about 0.90. Applicant respectfully submits that the 36 g to about 59 g of total

essential amino acids and/or conditionally essential amino acids per serving is a limitation that separate and compatible with the total essential amino acids and/or conditionally essential amino acids to total amino acids ratio. For example, both elements can be met by specifying an amount for the total essential amino acids and/or conditionally essential amino acids (between about 36 g to about 59 g) and then providing a corresponding remainder of amino acids (i.e. total amino acids = essential + non-essential) so that the total essential amino acids and/or conditionally essential amino acids:total amino acid ratio is about 0.6 (e.g. 0.6:1) to about 0.9 (e.g. 0.9:1). Based on at least these noted reasons, Applicant believes that Claims 3, 16 and 25 fully comply with 35 U.S.C. §112, second paragraph.

Accordingly, Applicant respectfully requests that the rejection of Claims 3, 16 and 25 under 35 U.S.C. §112 be withdrawn.

In the Office Action, Claims 3-4, 7-11, 13-14, 16 and 26 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,387,883 to Abbruzzese, et al. ("*Abbruzzese*"). Claims 1-2 and 23-24 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,387,883 to Madsen, et al. ("*Madsen*"). Claims 3-4, 7, 17, 25 and 27-28 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,420,342 to Hageman, et al. ("*Hageman*") in view of U.S. Patent No. 6,953,679 to Salvati, et al. ("*Salvati*"). Applicant respectfully disagrees with and traverses these rejections for at least the reasons set forth below.

Independent Claims 1-2 recite, in part, that leucine, in free and/or salt form, is present in an amount of at least about 25% to about 95% by weight based on the weight of total amino acids. Independent Claims 23-24 recite, in part, that leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of total amino acids. Independent Claims 3, 17, 25 and 28 recite, in part, leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein. Independent Claims 1-3, 17, 25 and 28 also recite, in part, a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90. In contrast, Applicant respectfully submits that the cited references fail to disclose or suggest every element of the present claims.

Applicant has found that when dietary intake is limited below the optimal level for physiological or patho-physiological reasons, a dietary supplement must be more effective than normal food intake in order to provide a benefit. This is because in this circumstance, when a dietary supplement is given, normal food intake is likely to be reduced by a calorically equivalent amount. Consequently, a supplement designed to limit cancer cachexia, for example, should stimulate muscle protein synthesis to a greater extent than normal food intake and should not interfere with the response to meal intake. Trials of conventional nutritional supplements in patients with cancer cachexia have failed to show appreciable benefit in terms of weight gain or quality of life. Accordingly, there is a need for effective nutritional approaches capable of treating, preventing or ameliorating the effects of tumor-induced weight loss due to, for example, cancer cachexia and/or anorexia.

Applicant has surprisingly found that a formulation containing free essential amino acids as compared to a formulation containing free essential and non-essential amino acids or intact protein alone is optimal. See specification, Examples 1-2. Applicant has also found that nutritional compositions comprising a mixture of essential amino acids in free form and/or in salt form that has particularly high amounts of leucine had a stimulatory effect on muscle protein synthesis. See specification, Example 3

In addition, Applicant has surprisingly and unexpectedly found that particularly useful compositions for promotion of muscle protein synthesis or controlling tumor-induced weight loss, such as cachexia, e.g. cancer cachexia, may be obtained by combining essential amino acids in free form and/or in salt form with intact protein. See specification, Example 2. The effect of such a combination is greater than the effect that can be achieved with either type of combination partner alone.

*Abbruzzese* fails to disclose or suggest that leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein as required by independent Claim 3. *Abbruzzese* also fails to disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 as required by independent Claim 3. The Patent Office admits same. See Office Action, page 5.

Applicant also submits that the skilled artisan would have no reason to arrive at the claimed invention in view of *Abbruzzese*. *Abbruzzese* is directed to methods and nutritional compositions for preventing and treating cachexia and anorexia. *Abbruzzese's* composition includes effective amounts of (1) ω3 fatty acids, such as α-linolenic acid, stearidonic acid, eicosapentaenoic acid, docosapentaenoic acid, docosahexaenoic acid or mixtures thereof; (2) branched-chain amino acids, such as valine, leucine, isoleucine or mixtures thereof; with or without reduced levels of tryptophan and 5-hydroxytryptophan; and (3) an anti-oxidant system selected from the group consisting of beta-carotene, vitamin C, vitamin E, selenium, or mixtures thereof. See *Abbruzzese*, column 3, lines 15-56. In the only example that utilizes leucine, *Abbruzzese* teaches an amino acid profile for his nutritional composition with leucine in an amount of 9.08 g/100 g protein (i.e. 9.08%), which is substantially lower than that of the present claims. See *Abbruzzese*, column 9, line 17. Moreover, in *Abbruzzese's* composition, the ratio of total essential amino acids and conditionally essential amino acids to total amino acids is 0.51, which is also much lower than that of the present claims. As a result, there is no teaching or suggestion to the skilled artisan to optimize the leucine range and amino acid ratios of *Abbruzzese* in accordance with that of the present claims in the absence of hindsight.

*Madsen* fails to disclose or suggest that leucine, in free and/or salt form, is present in an amount of at least about 25% to about 95% by weight based on the weight of total amino acids as required by independent Claims 1-2. *Madsen* also fails to disclose or suggest that leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of total amino acids as required by independent Claims 23-24. The Patent Office admits same. See Office Action, page 9.

Applicant also submits that the skilled artisan would have no reason to arrive at the claimed invention in view of *Madsen*. *Madsen* is directed to a nutritional composition that "comprises about 19.4 to 19.8% of leucine." Accordingly, *Madsen's* leucine level is lower than that of the claimed compositions. Moreover, *leucine* is one of many listed amino acids and *Madsen* fails to recognize or suggest any superior benefit from increased levels of *leucine* beyond what is taught. Consequently, the skilled artisan would have no reason to optimize the leucine range of *Madsen* in accordance with that of the present claims in the absence of hindsight.

*Hageman* and *Salvati* fail to disclose or suggest leucine, in free and/or salt form, is present in an amount of at least about 25% by weight based on the weight of intact protein as required by independent Claims 3, 17, 25 and 28. *Hageman* and *Salvati* also fail to disclose or suggest a ratio of total essential amino acids and, optionally, conditionally essential amino acids to total amino acids ranging from about 0.60 to about 0.90 as required by independent Claims 3, 17, 25 and 28.

Applicant further submits that the skilled artisan would have no reason to arrive at the claimed invention in view of *Hageman* and *Salvati*. *Hageman* generally describes a nutritional, pharmaceutical or dietetic preparation that includes effective amounts of ribose and folic acid, optionally combined with other components, such as niacin, histidine, glutamine, orotate, vitamin B6 and other components. See *Hageman*, column 5, lines 8-52. *Hageman* also discloses products having the following mixture of amino acids as beneficial for muscle growth when consumed in an amount of more than 2 and preferably more than 4 g per daily dose: 3-10 wt % histidine, 5-15 wt % isoleucine, 10-23 wt % leucine, 10-23 wt % lysine, 515 wt % methionine, 5-15 wt % phenylalanine, 5-15 wt % threonine. See *Hageman*, column 6, line 62-column 7, line 1. The maximum level of leucine of *Hageman's* composition is 23%, which is lower than that of the present claims.

*Salvati* generally describes fused cyclic compounds and methods of using such compounds in the treatment of nuclear hormone receptor-associated diseases such as cancer and immune disorders and pharmaceutical compositions containing such compounds. See *Salvati*, Abstract. *Salvati*, along with *Hageman*, lists *leucine* as one of many amino acids and fails to recognize or suggest any superior benefit from increased levels of *leucine* beyond what is taught. Consequently, the skilled artisan would have no reason to optimize the leucine range of *Hageman* and *Salvati* in accordance with that of the present claims in the absence of hindsight. As a result, there is no teaching or suggestion to the skilled artisan to optimize the leucine range or amino acid ratios of *Hageman* and *Salvati* in accordance with that of the present claims in the absence of hindsight.

Applicant respectfully submits that it is only with a hindsight reconstruction of Applicant's claimed invention that the Patent Office is able to even attempt to piece together the teachings of the prior art so that the claimed invention is allegedly rendered obvious. However,

the claims must be viewed as a whole as defined by the claimed invention and not dissected into discrete elements to be analyzed in isolation. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983); *In re Ochiai*, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995). One should not use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. *In re Fine*, 837 F.2d at 1075. (Fed. Cir. 1988).

In sum, the cited references fail to disclose or suggest every element of independent Claims 1-3, 17, 23-25 and 28. Moreover, the cited references fail to even recognize the advantages, benefits and/or properties of the nutritional compositions in accordance with the present claims. For at least the reasons discussed above, Applicant respectfully submits that Claims 1-3, 17, 23-25 and 28, along with the claims that depend from Claims 1-3, 17, 23-25 and 28, are novel, nonobvious and distinguishable from the cited references.

Accordingly, Applicant respectfully requests that the rejections of Claims 1-4, 6-14 and 16-28 under 35 U.S.C. §103 be withdrawn.

For the foregoing reasons, Applicant respectfully requests reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims that could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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